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REVIEW ARTICLE

Total Vascular Exclusion for Liver Resections: Pros and Cons

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Dramatic improvements in morbidity and mortality rates following liver resections have been reported in the past decade. Consequently, the indications for hepatectomy are becoming more liberal. Many techniques of liver resection with or without vascular clamping have been reported with excellent clinical results. Total vascular exclusion (TVE) of the liver during parenchymal transection has been advocated susceptible to increase the resectability of tumors that might not be safely approached by other techniques. Cirrhotic livers are probably more vulnerable to ischemic injury related to TVE than normal livers. The indications and technical and metabolic aspects of the technique are reviewed.
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KEY WORDS: total vascular exclusion; liver resection; hepatectomy; vascular occlusion

INTRODUCTION

At the end of this century hepatectomy is being performed widely as the procedure of choice for benign and malignant liver tumors [1–4]. The operative mortality has been considerably lowered over the last decade, due to better understanding of liver anatomy and physiology and improved techniques and technologies. Intraoperative ultrasonography has improved intraoperative imaging, whereas ultrasonic dissection and argon-beam coagulation have facilitated hemostasis. Simultaneous progress in intensive care support and anesthesiological management has considerably reduced the lethality of complications. However, intraoperative bleeding and hepatic reserve are the main risks in liver resection. Blood transfusion has been implicated as an independent factor in septic complications and associated with a decreased long-term survival in patients with liver metastases [5,6].

Several types of vascular occlusion have been advocated to reduce operative blood loss and render resectable centrally or near the inferior vena cava (IVC) located tumors [2,7–13]. The classic occlusion of the portal triad does not prevent hemorrhage or air embolus from either the IVC or the hepatic veins [5,8,14]. The routine practice of hepatic surgery in specialized liver units has led to the development of highly specific approaches to liver resections. Pringle maneuver and concomitant clamping of the inferior vena cava below and above the liver have recently been widely popularized. The technique can be found in the literature as total vascular exclusion (TVE) [7,15,16], hepatic vascular exclusion (HVE) [17–19], total vascular isolation (TVI) [20,21], or vascular isolation prior to parenchymal division (VIP) [11].

Although TVE is currently preferred for routine use in major liver resections by several hepatobiliary surgeons, the debate on the necessity and possible risks of liver vascular isolation still continues.

HISTORICAL BACKGROUND

The first successful excision of a liver tumor was achieved by Langenbuch in 1888 [22].

In 1908, Pringle first presented successful occlusion of

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the portal triad in humans [14]. He used this technique to arrest hemorrhage from an injured liver. Throughout many decades, occlusion of any portal vessels was considered not compatible with life due to the disappointing experimental results [23]. Experiments in dogs, which have poor pre-hepatic collateral circulation, have shown disastrous results after a prolonged Pringle maneuver [24]. Portal triad cross clamping was then extended to 30 min in humans only after body hypothermia [25,26].

In was only in 1960s, that Heaney et al. reported successful vascular isolation in normothermic patients [27]. Intrapericardial control of the suprahepatic inferior vena cava, suprarenal clamping of the infrahepatic IVC, portal triad occlusion, and clamping of the aorta below the diaphragm was then proposed [28]. During the following years, progress in the literature was slow, until 1978 when Huguet showed that the liver can withstand normothermic ischemia for a prolonged period [8]. Up to this period, a hypothermic perfusion technique was used for hepatic resections under vascular isolation [29]. A few years later, similar results in emergency liver surgery came to establish the techniques of vascular exclusions [30]. Modern liver resection techniques, with the use of complete inflow and outflow isolation, evolved further with techniques used in liver transplantation [2,7,31]. TVE was the application of the hepatectomy dissection used in transplantation to conventional liver surgery. The experience gained using TVE by surgical and anesthesia teams resulted in acceptance and broader practice of the technique [15].

TECHNICAL CONSIDERATIONS

The standard approach is a bilateral subcostal incision with upper midline extension [1,11,21]. In less than 1% of liver resections, when the volume of the liver mass precludes a safe approach to the suprahepatic vena cava, a thoracic extension has been suggested [19]. The liver should be mobilized by dividing the right and left triangular ligaments, as well as the falciform and coronary ligaments. The hepatoduodenal ligament is encircled and careful search for an anomalous left hepatic artery is made. Separate clamping is essential to avoid liver congestion during the TVE period.

The infrahepatic IVC has to be clamped superiorly to the right renal vein. The right adrenal vein should be ligated unless the inferior clamp can be applied above its junction with the IVC [7,19,32]. The suprahepatic IVC is dissected, carefully taking care not to damage the phrenic veins, which may drain directly into a main hepatic vein. The phrenic veins are ligated only in cases of low insertion into the IVC [16]. The lateral aspects of the suprahepatic IVC have to be exposed, and the vein is encircled with a sling [21]. A trial dissection of the hepatic veins is performed and if an easy extrahepatic ligation is feasible, this is done and the relevant hepatic vein tied in continuity with a silk ligature. Total vascular exclusion is achieved by clamping the inflow portal triad and then the infrahepatic cava, followed by the suprahepatic cava.

Control of the right hepatic vein outside the liver is dangerous when dealing with a large tumor of the right lobe. TVE enables the surgeon to transect the hepatic vein from within the liver parenchyma when the transection is almost completed. Hepatotomy with a scalpel has been described by Habib et al. [16], leaving a flat liver surface where severed vessels and ducts are easily exposed and sutured.

After completing the parenchyma transection and prior to removing the clamps, the infrahepatic clamp can be partially released to flush air that might have been trapped and to check for caval integrity. The clamps are then removed in the reverse order to which they were initially placed. Total vascular exclusion cannot be applied in an intermittent fashion as the caval flow cannot be interrupted and released sequentially [33].

Stephen et al. have recently proposed aortic occlusion and TVE as a definitive method to allow a bloodless hepatic resection [34,35]. They suggested that TVE without aortic occlusion is only partially successful in controlling hemorrhage as they experienced moderate blood loss from the uncontrolled tributaries of the IVC [29,34]. Application of the aortic clamp reduces blood flow through the lower half of the body and further reduces venous bleeding [31]. Nevertheless, isolation of the supraceliac aorta has been challenged as it can cause spinal cord ischemia, thrombotic ischemic injury at distant sites [20], or ventricular arrhythmias [5].

Several techniques have been suggested by liver surgeons not using TVE. Lin has advocated the finger fracture technique and the use of a liver clamp although his technique seems hard to apply [36]. Hodgson and Delgucicio invented the Cavitron ultrasonic surgical aspirator (CUSA) in an effort to decrease the blood loss during major liver resections. The liver parenchyma is divided whereas the vessel walls and biliary ducts are not fragmented by the ultrasound but skeletonized and ligated [37].

HEMODYNAMIC CONSEQUENCES

The liver is the largest single organ and has a vascular compliance approximately 10 times higher than the compliance of the total systemic vasculature. Its plethoric vasculature plays an intensive role in cardiovascular dynamics and consummates a myriad of metabolic and detoxifying functions [38]. Inferior vena cava carries two thirds of the cardiac output back to the heart [39].

Hemodynamic alterations after liver inflow and outflow occlusion are now well investigated. Exclusion of both afferent and efferent blood supply creates a massive hepatic sequestration of blood. Delva et al. showed a decrease in cardiac index of approximately 50% [40].

Despite this decrease, the mean arterial pressure is maintained due to a dramatic increase in the systemic vascular resistance [41]. Urine output was found to be reduced and a minimal rise in serum creatinine levels has been noticed during TVE without any cases of acute renal failure [7,15,16,20]. An intravenous preloading with fluids has been suggested to minimize the consequences of the decrease in venous return and cardiac index [1,41,42]. Additionally, trial clamping of the IVC and the portal triad before proceeding to resection has been recommended [7,16,40]. If the mean arterial pressure decreases by more than 20%, the clamps are released and intravascular volume is corrected. Release of the clamps is followed by a substantial increase of venous return and a dramatic increase of diastolic pulmonary arterial pressure and the pulmonary capillary wedge pressure gradient [40]. The risk of pulmonary edema at that time is less significant than previously believed [41,43].

Extracorporeal venovenous bypass from the infrahepatic vena cava to the axillary vein has been shown to provide adequate central venous filling without a significant decrease in cardiac output [33,44,45].

Total vascular exclusion can be tolerated in a normal liver for at least 60 minutes [1,7,8,46,47]. This can be explained by the presence of large collateral venous channels in humans, such as the azygos vein [39].

The use of the TVE in cirrhotics had discouraging results. These patients cannot tolerate the hemodynamic alterations and the recirculation injury to the ischemic liver following portal occlusion [13,48,49]. The value of venovenous bypass during TVE has been emphasized for this patient population [13,50].

However, Nagasue et al. have presented occlusion of both hepatic inflow and outflow in cirrhotics for at least 30 minutes without any intraoperative complication, although this material included mainly segmental liver resections [51]. Furthermore, Hannoun et al., after cooling of the hepatic parenchyma, performed major hepatic resection in patients with diseased livers using HVE for longer than 1 hour without increased morbidity or mortality [18]. Nevertheless the existence of unexpected collateral vessels in a cirrhotic liver can render the blood loss high [13]. This could be avoided by a concomitant with the TVE occlusion of the aorta, first proposed by Heaney et al. [27]. More recently, the above technique was proposed to prevent the engorgement of the intestine and lower half of the body [34]. However, the debate is that the approach to the supraceliac aorta may be difficult, whereas unexplained ventricular arrhythmias have been recorded [39]. The dangers of concomitant aortic occlusion and total vascular occlusion implicating more acidemia can be particularly evident in massive liver resections and in diseased liver with reduced baseline reserve.

Cheung et al. have stressed the advantage of partial clamping of the inferior vena cava over total clamping during liver transplantation. In patients who underwent partial clamping of the vena cava, the mean pulmonary artery pressure and cardiac output decreased but not significantly as in patients with total clamping of the vena cava [52].

On the other hand, techniques such as lowering of central venous pressure by fluid restriction and nitroglycerine infusion, to facilitate dissection of hepatic veins without TVE, have their proponents [53].

METABOLIC DISTURBANCES

A great variety of factors could be responsible for the extent of biochemical alterations following liver resection either by portal triad clamping or total vascular exclusion.

Regenerative phenomena, mechanical damage to hepatocytes at the sites of resection, prolonged ischemia, and reperfusion injury have been considered as causes of hyperenzymemia [7,54]. Bilirubin, aspartate aminotransferase (AST), and prothrombin time (PT) alteration after hepatectomy have been associated with several factors including blood transfusion, liver vascular isolation, and the amount of liver parenchyma removed [7,55–57]. The exact effect of TVE per se on postoperative biochemical changes is difficult to be evaluated as blood and fresh frozen plasma (FFP) transfusion, underlying liver disease, and postoperative complications are known to contribute in these alterations [58,59]. It has been suggested that portal triad clamping per se can cause either cell ischemia or “deleterious” reperfusion of pooled portal blood [60]. However, in humans the concept of poor tolerance of the liver to warm ischemia has been challenged and it has been shown that liver vascular exclusion can be performed safely for up to 1 hour [15,61,62]. Systemic metabolic acidosis is sometimes encountered, especially immediately after clamp release, but acid-base balance returns to normal in less than 30 minutes [40].

The duration of TVE or pedicle inflow occlusion [57] was shown to have a significant correlation with the rise in postoperative serum aspartate aminotransferase (AST) levels [7,11]. In other series, such a correlation was not found [16,20]. A relationship between the elevations in the prothrombin time (PT) and the number of liver segments resected as well as the duration of TVE has been observed [16,20].

Liver ischemia following vascular clamping is associated with inadequate adenosine triphosphate (ATP) formation and impaired cell membrane integrity and protease activation. Accumulated evidence shows that reperfusion damage is due to toxic free radicals released secondary to oxygen restoration in anoxic tissue. Cytokines such as tumor necrosis factor-a, interleukin-1, and interleukin-6 play key role in this cascade of events [63,64].

Others have postulated that the remarkable increase of thromboxane B2 during hepatectomy may play an important role in the development of “reperfusion” liver damage following hepatic resection. The preventive role of prostaglandin E1 has not yet been established [65]. Theoretically, liver vascular isolation could predispose to both hepatocyte ischemia and reperfusion injury. However, in terms of liver function tests such a correlation is still controversial [7,16,20,47,57,66].

CURRENT TRENDS

Total vascular exclusion is reported to have the advantage of parenchymal division in a completely bloodless field so that meticulous identification and ligation of vascular and biliary radicals can be accomplished [16,46]. Over the last years, indications for applying the TVE technique have been expanded and in some institutions TVE is routinely accomplished during major hepatic resections or where the lesion is close to the inferior vena cava or the liver hilus [11,16,61,62]. The above technique is not necessary in anteriorly or peripherally placed lesions. In these cases, Pringle’s maneuver is sufficient [5,7,16]. Operations as combined hepatic and vena caval resection for malignant tumors are absolute indications for total vascular exclusion [59,67].

Another indication for TVE is liver trauma, when effective control of the bleeding cannot be obtained by packing or portal triad clamping [68]. Cross-clamping of the aorta may be required in patients with major trauma but the hemodynamic intolerance and the potential hazards of the maneuver has limited the use for this approach [20].

It appears that satisfactory TVE depends on adequate surgical technique [8], after a slight vascular overload [7,16,40,41]. Incomplete vascular isolation can cause blood sequestration in the liver during transection [8]. The hemodynamic tolerance is also satisfactory, despite the drop in the cardiac index [40,41].

Aortic clamping [16,50] is inappropriate in view of the known complications [28] and the excellent hemodynamic tolerance obtained without aortic occlusion.

Japanese surgeons have strictly limited the patients who undergo liver resections under TVE as they found systemic circulatory disturbance in the population of cirrhotic patients. Although TVE has been used successfully in selected cirrhotic patients, it seems that prospective studies will be required to define the parameters for use of this technique in cirrhosis [69]. Okuda et al. recently proposed the hemihepatic vascular occlusion method, interrupting the backflow from the vena cava into the hepatic vein with the balloon of a foley catheter [10]. Furthermore, Makuuchi et al. have advocated hemihepatic occlusion of the relevant portal vein and hepatic artery, on the basis that prolonged Pringle maneuver itself can cause hepatic ischemia, liberation of endotoxins, and intestinal congestion in cirrhotics [10,48,70]. However, in the non-cirrhotic patients, a good metabolic tolerance of the liver to prolonged normothermic ischemia has been reported [40,46,71].

Postoperative morbidity is not reduced after liver resections under TVE [12,16]. It remains high with a complication rate from 27 to 50% [2,6,7,12,16,20,53,70,72,73].

A recent prospective randomized trial comparing intermittent clamping of the portal triad and TVE has demonstrated a higher pulmonary complication rate of the latter technique [17]. However, this study suffers from a major selection bias, excluding patients with tumors near hepatic veins or IVC.

A significant rate of pleural effusions [7,16,73] can be identified in many hepatectomy series. Extensive mobilization of the liver, necessary for a safe dissection of the suprahepatic IVC, could predispose for subphrenic fluid collections and postoperative pleural effusions [5]. The overall hospital mortality is currently in the same range of less than 5% as published in series from institutions where the conventional techniques are used [4,7,11,16,20,55,68,74–76].

The use of TVE often reflects the difficulty of surgical management either in major liver resection or in resection of small tumors located near the inferior vena cava or hepatic veins. In most series, the technique has been found to be safe, with low mortality, acceptable morbidity, and a remarkable limitation of blood loss and transfusion requirements.

CONCLUSIONS

A significant proportion of liver resections may be carried out with portal triad clamping alone. Total vascular exclusion could be applied for either large or centrally and posteriorly located tumors. The technique is an absolute indication for operations, as combined hepatic and inferior vena cava resection. This method must be applied by experienced hepatobiliary surgical teams to minimize the risks of vena cava injury during dissection and hemodynamic instability during vascular occlusion of the liver.

It is not clear whether patients with liver cirrhosis can tolerate liver ischemia due to TVE, within certain limits. Venous bypass, while seldom needed, may allow extension of the period of TVE in older or cirrhotic patients who may not tolerate either the reduction in cardiac index or the reperfusion hepatocyte injury.

Despite the obvious advantages of the total vascular exclusion technique regarding the intraoperative blood loss, the technique has not been established in randomized clinical trials. For the time being, the ability to resect the liver safely is related to the extensive knowledge of

liver anatomy, the use of ultrasonic dissector (CUSA), as well as the availability of various types of liver vascular exclusion techniques.

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COMMENTARY

Increased understanding of hepatic anatomy, advances in imaging, and improved perioperative management have greatly improved the outcome after hepatic resection. Mortality rates for hepatic resection are now 2–5%, with perioperative transfusion requirements as low as 0–2 units for most resections. Since resection for both primary and metastatic liver tumors offers the best option for survival and hepatic resection can be accomplished with low morbidity and mortality rates, indications for resection have been liberalized. Tumors once deemed technically unresectable are not being removed with more frequency. The article by Zografos and colleagues describes the technique of total vascular exclusion (TVE) for hepatic resection of these difficult lesions. They also review the hemodynamic and metabolic consequences and suggest indications for TVE [1].

As the authors state, the vast majority of hepatic resections can be performed with *selective* inflow and outflow occlusion. This technique allows safe hepatic resection with minimal metabolic or hemodynamic consequences without compromising oncologic principles. Inflow control is usually accomplished by either a Pringle maneuver or extrahepatic ligation of the portal vein and hepatic artery. Recently, the use of selective intrahepatic pedicle ligation of inflow vessels guided by intraoperative ultrasound for segmental resection has been advocated [2]. Outflow control of the hepatic veins can be performed either intrahepatically at the completion of parenchymal transection or, more preferably, extrahepatically prior to parenchymal transection to minimize blood loss.

While the technique of total vascular exclusion as described by the authors provides another method of inflow and outflow control, the indications for its use remain poorly defined. The authors state that direct invasion of the IVC or hepatic veins is an absolute indication for TVE. While this may be true, this scenario is quite rare. Metastatic lesions rarely invade the vena cava and can often be dissected free without vascular resection. In addition, for direct extension of tumor into the intrahepatic portion of the vena cava, a tangential excision may be performed with a side biting vascular clamp without the need for TVE. While primary liver tumors are more likely to invade the vena cava and hepatic veins, the presence of cirrhosis may preclude the use of TVE, since these livers are more vulnerable to ischemic injury.

While its routine application is not indicated, the authors correctly state that the technique of TVE for hepatic resection may be a useful one in highly selective cases.

Although size may not constitute an absolute indicate for TVE, inopportunely placed small lesions may. A lesion situated at the confluence of the hepatic veins may require TVE for safe resection. Importantly, for these rare cases, TVE should be performed by a dedicated team consisting of experienced hepatic surgeons, anesthesiologists, and critical care personnel.

For the time being, most hepatic resections can be safely performed with selective inflow and outflow control. However, as the willingness and comfort of surgeons to approach locally advanced hepatic lesions increase, the need for TVE in these selective cases may follow.

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